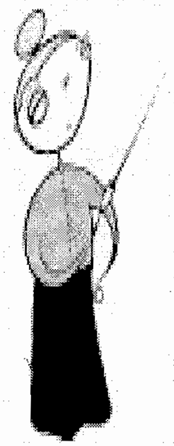
APPLIED ANATOMY OF THE KIDNEY / NEPHRON



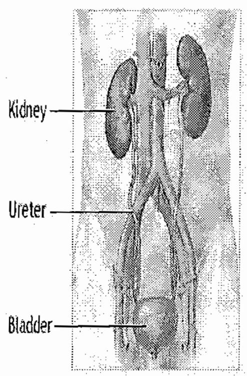
APPLIED PHYSIOLOGICAL ANATOMY OF THE KIDNEY / NEPHRON

FUNCTIONAL ANATOMY OF KIDNEY / NEPHRON

- Kidneys are a pair of excretory organs situated on the posterior abdominal wall on each side of the vertebral column.

Located mainly in the lumbar region

Extend vertically from the upper border of the T_{12} vertebra to L_3 vertebra. The right kidney is slightly lower than the left.



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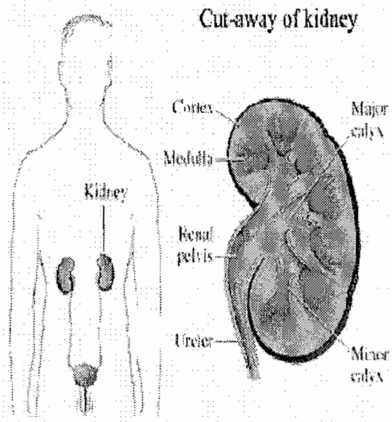
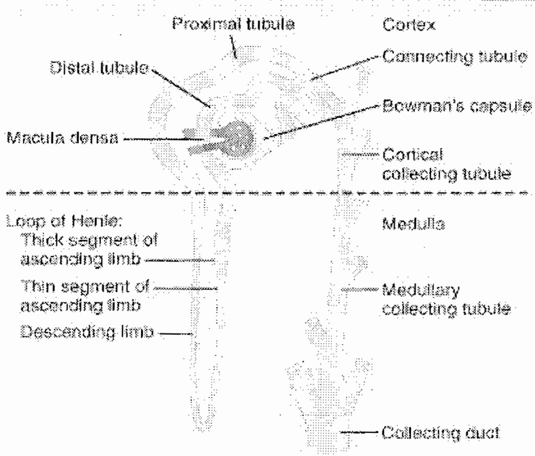
FUNCTIONAL ANATOMY OF KIDNEY / NEPHRON

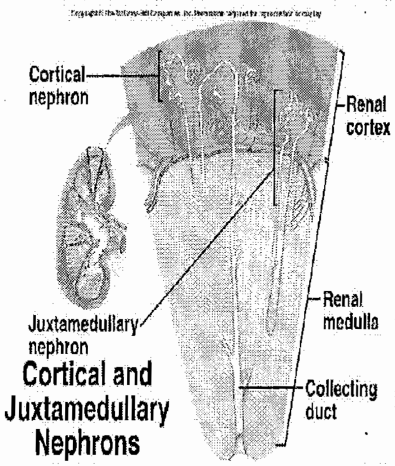
Each kidney is bean shaped. They are 12 cm long , 6 cm broad and 3 cm thick. The weight of each kidney is 150 gm in males and 135 gm in female.

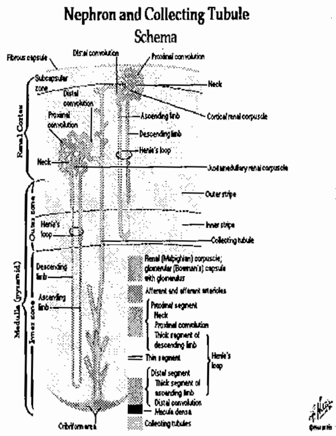


FUNCTIONAL ANATOMY OF KIDNEY / NEPHRON

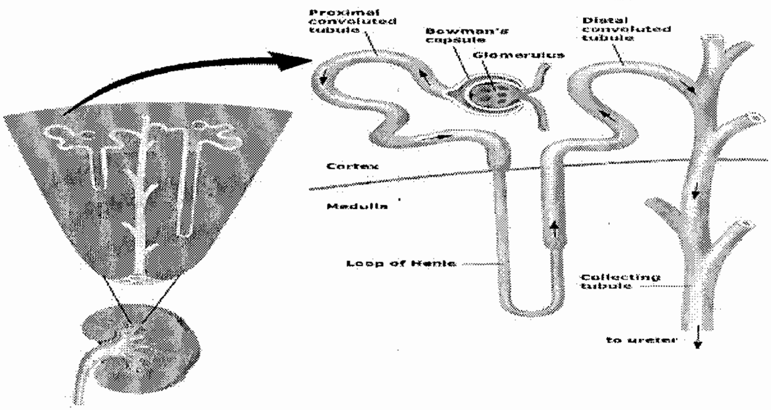


NEPHRON





NEPHRON



- Superficial (cortical [85 %]: Capable of forming dilute urine
- Juxtamedullary [15 %]: Capable of forming concentrated 300 mOsm/kg) urine

NEPHRON

Cortical nephrons: These are nephrons whose glomeruli lie close to the surface of the kidneys. These nephrons comprise about 85% of the nephrons in the kidneys and have glomeruli located in the renal cortex.

The cortical glomeruli is small and have short thin segments and their loops of Henle penetrate a short distance into the outer portion of the medulla.

NEPHRON

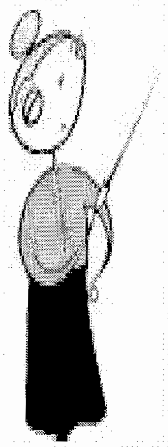
Juxta medullary nephrons

The glomeruli of juxta medullary nephron lies deep in the renal cortex near the medulla. These nephrons comprise of about 15% of nephrons and have long thin segments and their loops of Henle penetrate deep into the inner portion of the medulla.

FUNCTIONS OF KIDNEY

- Excretion of waste products [creatinine, urea]
- Regulation of water [extracellular fluid volume]
- Maintenance of Electrolyte balance [Na+, K+, HCO3, Ca++]
- Regulation of arterial pressure and Regulation of blood pH
- Secretion, metabolism, and excretion of hormones
- Hormone production [Erythropoietin, Renin]
- Activation of Vitamin D

JUXTAGLOMEULAR APPARATUS [JGA]

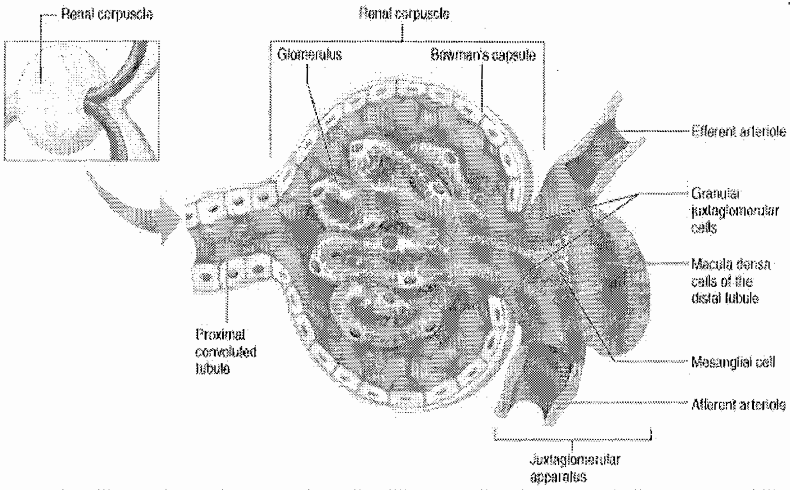


JUXTAGLOMEULAR

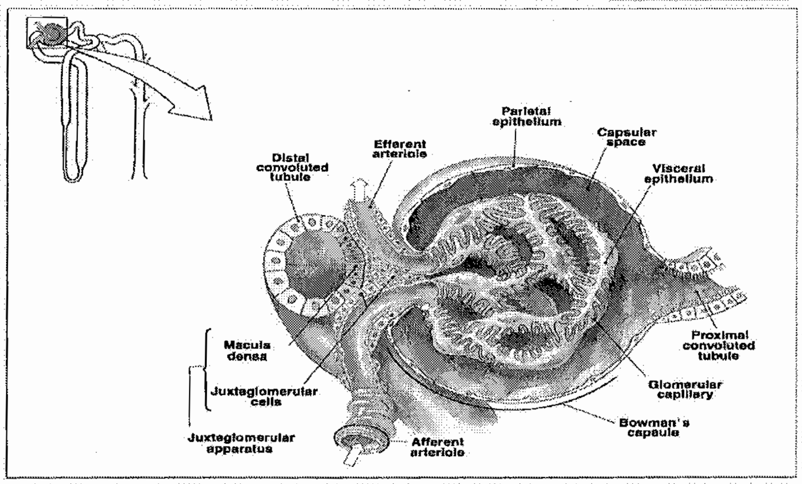
APPARATUS

[JGA]

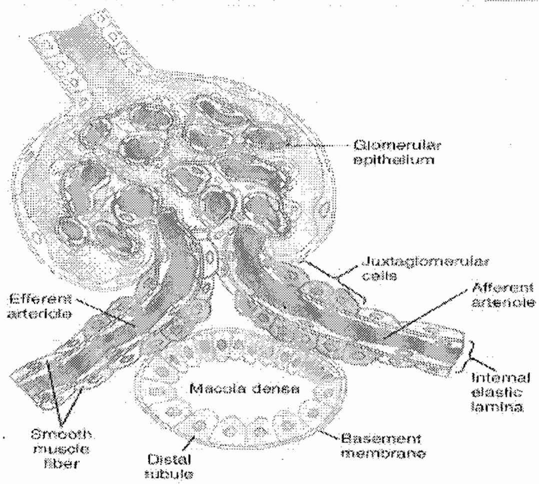
JUXTAGLOMEULAR APPARATUS [JGA]



JUXTAGLOMEULAR APPARATUS [JGA]



JUXTA GLOMERULAR APPARATUS



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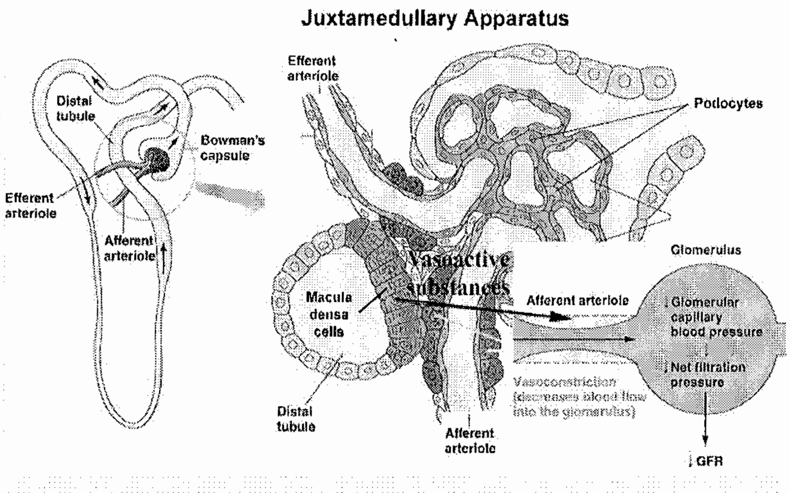
JUXTRAGLOMEULAR APPARATUS [JGA]



JUXTA GLOMERULAR APPARATUS

JUXTA GLOMERULAR APPARATUS

This is the combination of structures/cells lying close to the glomerulus. The components of the juxta-glomerular apparatus play a role in the control of blood pressure, renal blood flow, Electrolytes balance and Erythropoiesis.

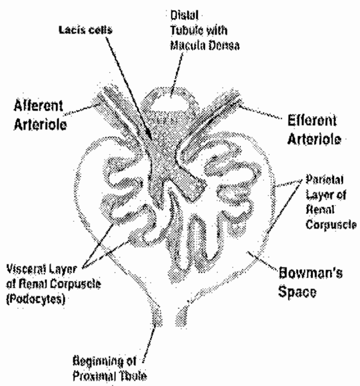
Structures forming the juxtaglomerular apparatus

- Macula densa of the distal convoluted tubule
- The lacis cells
- The JG cells

JUXTRA GLOMERULAR APPARATUS

Macula densa

The macula densa is a group of modified epithelial cells in the portion of the distal convoluted tubule lying in contact with the afferent glomerular vessel of the same nephrons.



JUXTRA GLOMERULAR APPARATUS

The lacis cells: These cells also known as polkissen cells or Goor maghtigh's cells.

These cells are formed mainly by a granular.

These cells lie in close contact with the macula densa and also within the vascular pole formed by the afferent and efferent glomerular vessels.

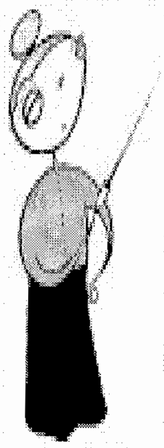
JUXTRA GLOMERULAR APPARATUS

The juxta glomerular cells

These cells are granular epitheloid cells located in the media of the proglomerular portion of the afferent and occasionally the efferent arterioles.

Granulation in the juxta glomerular cells is related with the presence of secretable renin. Renin secretion is determined by the degree of stretch of the afferent glomerulus and also by the Na^+ concentration of the macula densa.

GLOMEULAR MEMBRANE



GLOMEULAR MEMBRANE

GLOMERULAR MEMBRANE

The glomerular capillary membrane is similar to that of other capillaries, except that it has three (instead of the usual two) major layers:

[i] Endothelial layer of the glomerular membrane has a fenestrae.

[ii] The basement membrane.

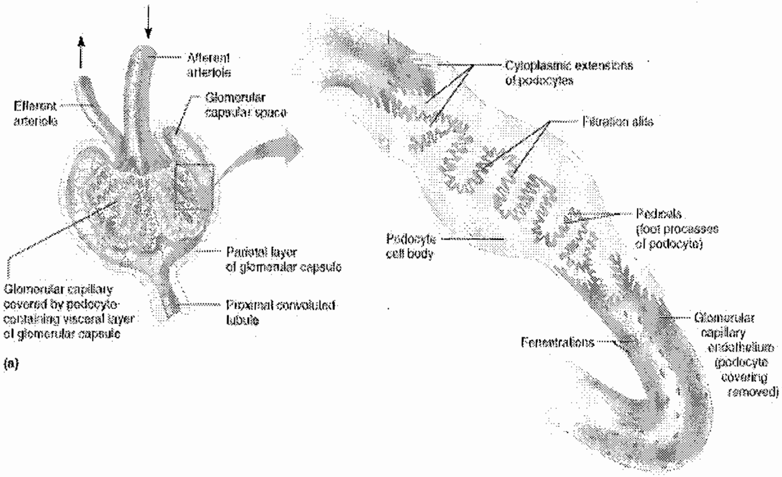
[iii] A layer of epithelial cells [podocytes] on the outer surfaces of the glomerular capillaries which have pores.

GLOMERULAR MEMBRANE

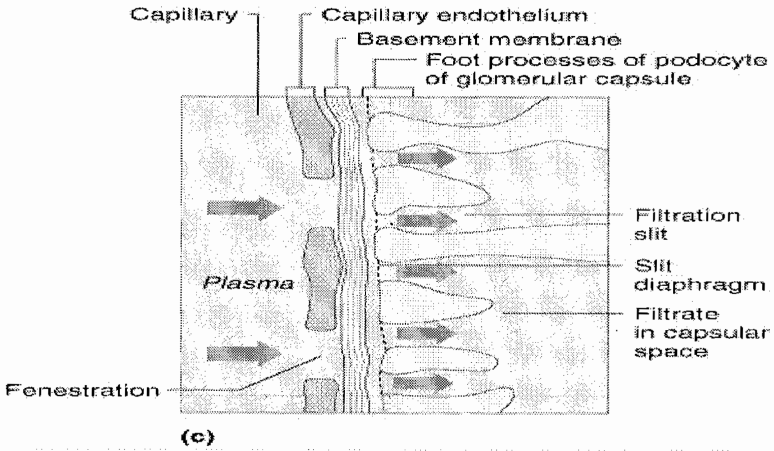
Fenestrae: The capillary endothelial cells lining the glomerulus are perforated by literally thousands of small holes called fenestrae.

Slit pores: Epithelial layer is not a continuous layer but instead consists mainly of fingerlike projections that cover the basement membrane, these fingers form slits which are called slit pores.

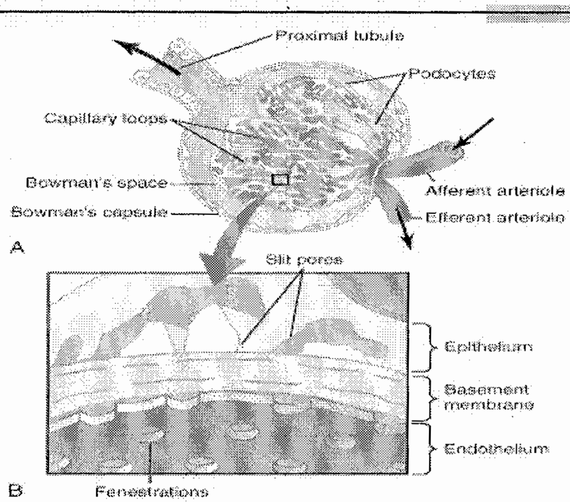
GLOMERULAR MEMBRANE



GLOMERULAR MEMBRANE



GLOMERULAR MEMBRANE



GLOMERULAR MEMBRANE

- Glomerular permeability: The glomerular filtrate passes through three different layers i.e. endothelial layer, basement membrane, and epithelial layer
- Each of these layers is several hundred times as porous as the usual capillary membrane.
- Despite this tremendous permeability of the glomerular membrane, it has an extremely high degree of selectivity for the sizes of molecules that it allows to pass.

GLOMERULAR MEMBRANE

Does proteins pass through glomerular membrane

Glomerular membrane is completely impermeable to all plasma proteins.

Causes of impermeability [Pores size]: Pores of the glomerular membrane are large enough to allow neutral molecules with diameter up to 8 nanometers to pass through. Even though the molecular diameter of the plasma protein (albumin) molecule is only about 6 nanometers, it still not pass through the membrane.

GLOMERULAR MEMBRANE

DOES PROTEINS PASS THROUGH GLOMERULAR MEMBRANE

Negative charge:

The basement membrane of the glomerular pores are lined with a complex of proteoglycans that have very strong -ve electrical charges. Similarly the plasma proteins have -ve charges.

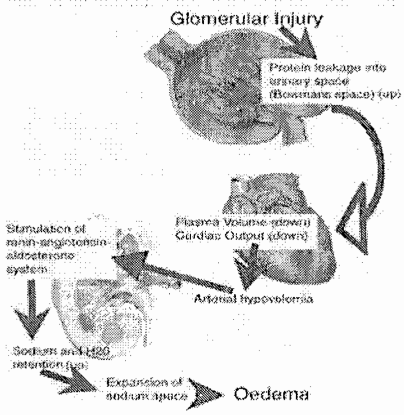
Therefore electrostatic repulsion of the molecules by the pore walls keeps virtually all protein molecules > 69,000 molecular weight from passing through.

GLOMERULAR PERMEABILITY

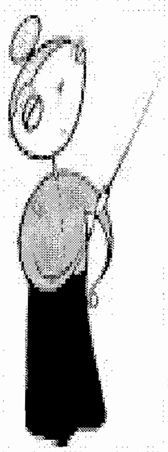
- The permeability of the glomerular capillaries is about 50 times that of the capillaries in skeletal muscle.
- Neutral substances with effective molecular diameters of less than 4 nm are freely filtered. Filtration of neutral substances with diameters of more than 8 nm approaches zero.
- Sialoproteins in glomerular capillary wall are negatively charged. The negative charges repel negatively charged substances in blood

GLOMERULAR PERMEABILITY
Proteins Leakage

- The presence of significant amounts of albumin in the urine is called **albuminuria.**
- In nephritis, the negative charges in the glomerular wall are dissipated, and albuminuria can occur for this reason without an increase in the size of the "pores" in the membrane.



GLOMEULAR FILTATION RATE



GLOMEULAR FILTRATION RATE

GLOMEULAR CAPSULE

- **Glomerulus:** Each nephron contains clumps of capillaries. These capillaries are highly porous and allow large amounts of solute-rich, virtually protein-free fluid filtrate to pass from the blood into the glomerular capsule
- **Glomerular capsule/ Bowman's capsule:** A cup-shaped structure (a blind pouch) that encloses the glomerulus. First part of the nephron that moves fluid out of the body.

GLOMERULAR FILTATION

Glomerular Filtration

The First Step in Urine Formation: Urine formation begins with filtration of large amounts of fluid through the glomerular capillaries into Bowman's capsule.

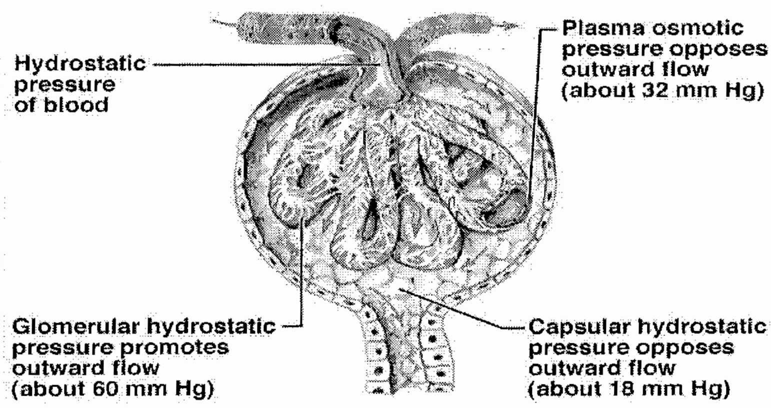
Composition: The glomerular capillaries are relatively impermeable to proteins, so that the filtered fluid [called the glomerular filtrate] is essentially protein-free and devoid of cellular elements, including red blood cells.

GLOMEULAR CAPSULE

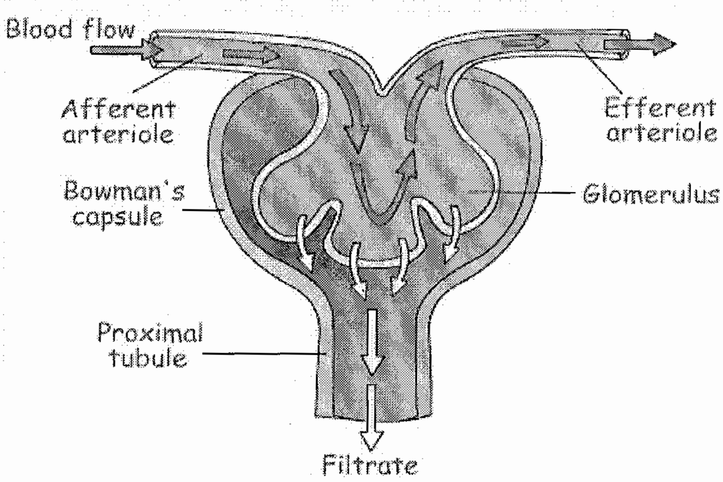
- Afferent arterioles: Feed into the glomerular capillary bed. Has a larger diameter than the efferent arteriole
- This is one of the reasons that blood pressure is high in the glomerulus. The elevated blood pressure is needed to force fluid out of the bloodstream and into the nephron.
- Efferent arterioles: Carry the newly filtered blood away from the glomerulus. Narrower diameter than the afferent vessels keeps glomerular pressure high.

GLOMERULAR FILTATION RATE

Glomerular Filtration Rate

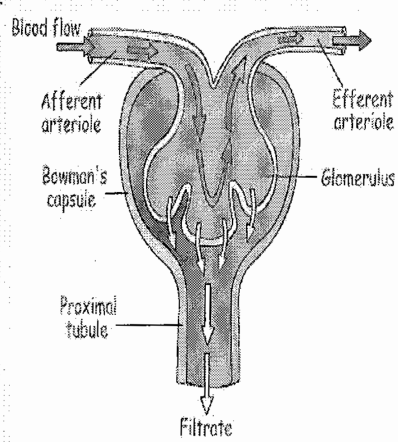


GLOMERULAR FILTRATION



GLOMERULAR FILTRATION RATE GFR

Definition: This is the fluid that filters through the glomerulus into the Bowman's capsule per minute.



GLOMERULAR FILTATION RATE GFR

- Normal GFR: The GFR in an average-sized normal man is approximately 125 mL/min. OR 180 L/d
- Its magnitude correlates fairly well with body surface area
- In females 10% lower than those in men even after correction for surface area.
- The normal urine volume is about 1 L/d. Thus, 99% or more of the filtrate is normally reabsorbed:
- GFR= Filtration pressure x Filtration co-efficient.

FILTRATION FRACTION (FF)

Filtration fraction (FF) This is the fraction of the renal plasma flow that becomes glomerular filtrate. It is about 19-20%.

- The ratio of the Glomerular filtration rate to the renal plasma flow (RPF).
- The **filtration fraction**, is normally 0.16–0.20.
- The GFR varies less than the RPF. When there is a fall in systemic blood pressure, the GFR falls less than the RPF because of efferent arteriolar constriction, and consequently the filtration fraction rises.

PRESSURES ACTING ON GLOMERULAR FILTATION

- Dynamics of filtration: The following are the pressures involved in the formation of glomerular filtrate.
- Glomerular pressure: It is the average pressure in the glomerular capillaries. This pressure promotes filtration through the glomerular membrane.
- It is about 60 mm Hg.

PRESSURES ACTING ON GLOMERULAR FILTATION

- The pressure responsible for filtrate formation
- NFP equals the glomerular hydrostatic pressure (HP_g) minus the oncotic pressure of glomerular blood (OP_g) combined with the capsular hydrostatic pressure (HP_c)
- $NFP = HP_g - (OP_g + HP_c)$

PRESSURES ACTING ON GLOMERULAR FILTATION

- Filtration Pressure is the force that drives the fluid and its dissolved substances through the glomerular filter

Net Filtration pressure NFP: [Net Hydrostatic Pressure NHP] is the difference between three pressures:

1. Glomerular (blood) hydrostatic pressure [GHP or GBHP]=60
2. Bowman's Capsular Hydrostatic Pressure [CHP]=18
3. (Blood) Colloid Osmotic Pressure [BCOP]=32

The relationship can be expressed by: NPF=GBHP-(CHP+BCOP)

PRESSURES ACTING ON GLOMERULAR FILTATION

1. Glomerular (blood) hydrostatic pressure [GHP or GBHP] =60 mmHg
2. Bowman's Capsular Hydrostatic Pressure [CHP] =18mmHg
3. (Blood) Colloid Osmotic Pressure [BCOP] =32 mmHg

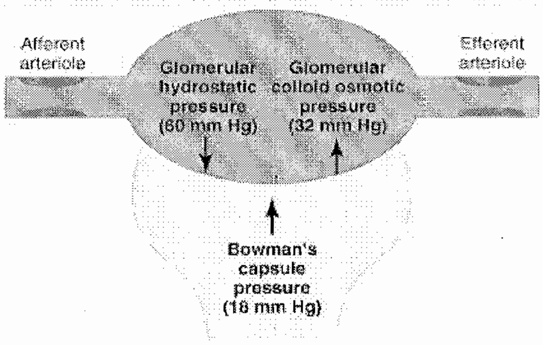
The relationship can be expressed by:

NPF= GBHP- [CHP + BCOP]

60- [18 + 32 =50]

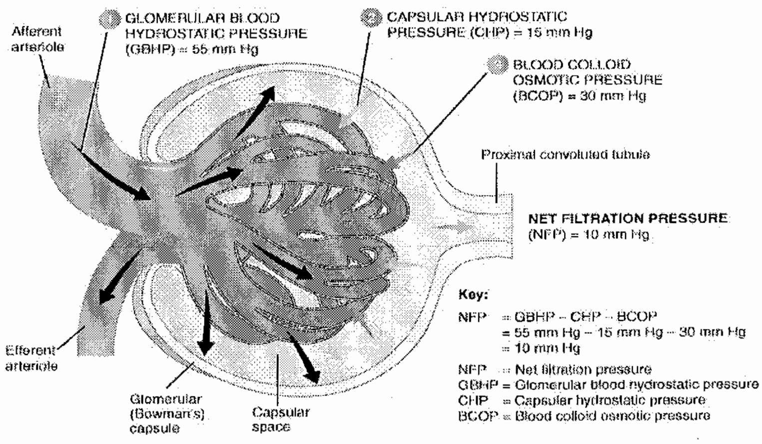
NPF 60-50=10 mmHg

NET GLOMERULAR FILTRATION PRESSURE

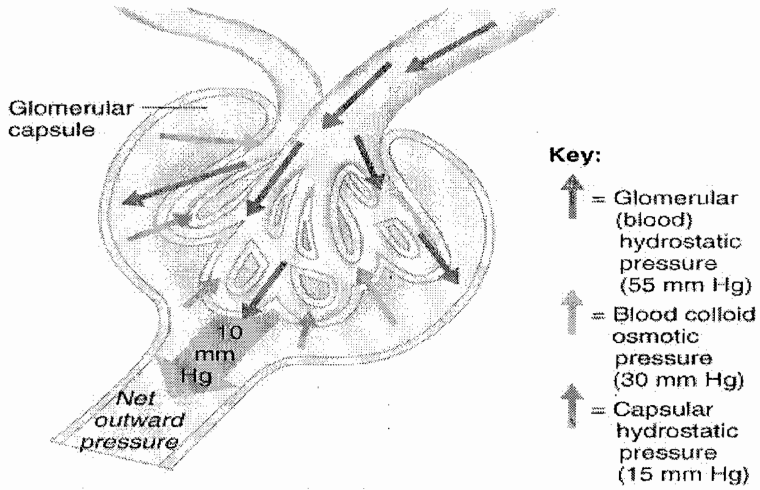


Net filtration pressure (10 mm Hg) = Glomerular hydrostatic pressure (60 mm Hg) − Bowman's capsule pressure (18 mm Hg) − Glomerular oncotic pressure (32 mm Hg)

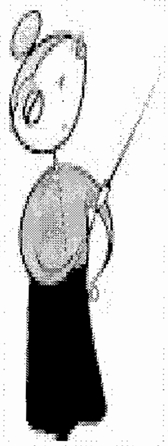
NET GLOMERULAR FILTATION PRESSURE



NET GLOMERULAR FILTATION PRESSURE



REGULATION OF GLOMERULAR FILTATION RATE



REGULATION OF

GLOMERULAR FILTATION

RATE [GFR]

REGULATION OF GLOMERULAR FILTRATION

- The factors governing filtration across the glomerular capillaries are the same as those governing filtration across all other capillaries [Dynamics of Blood]

Example:

- Size of the capillary bed
- The permeability of the capillaries
- The hydrostatic and osmotic pressure gradients across the capillary wall.

REGULATION OF GLOMERULAR FILTRATION

$$GFR = K_f[(P_{GC} - P_T) - (\pi_{GC} - \pi_T)]$$

- K_f: The glomerular ultrafiltration coefficient, is the product of the glomerular capillary wall (ie, permeability)
- P_{GC}: Osmotic pressure of the plasma in the glomerular capillaries
- P_T : Hydrostatic pressure in the tubule
- $_{GC}$: Osmotic pressure of plasma in the glomerular capillaries,
- $_T$ the osmotic pressure of the filtrate in the tubule.

REGULATION OF GLOMERULAR FILTRATION

- If the GFR is high: Fluid passes very rapidly, kidneys are unable to reabsorb needed substances and lost in the urine
- If the GFR is low: Fluid passes very slowly most of the substances are reabsorbed, kidneys fail to eliminate essential waste products.
- Three mechanisms control the GFR
  - Renal autoregulation (intrinsic system)
  - Neural controls
  - The renin-angiotensin system (hormonal mechanism)

REGULATION OF GLOMERULAR FILTRATION

INTRINSIC CONTROL:

- In normal conditions, renal autoregulation maintains nearly constant GFR
- Autoregulation entails two types of control
  - Myogenic: responds to changes in pressure in the renal blood vessels
  - Tubuloglomerular feedback: Senses changes in the juxtaglomerular apparatus

REGULATION OF GLOMERULAR FILTRATION

Sympathetic Nervous System Control:

- When the SNS is at rest:
  - Renal blood vessels are maximally dilated
  - Autoregulation mechanisms prevail
- Under stress:
  - Norepinephrine is released by the SNS
  - Epinephrine is released by the adrenal medulla
  - Afferent arterioles constrict and filtration is inhibited
- The SNS also stimulates the renin-angiotensin mechanism

REGULATION OF GLOMERULAR FILTRATION

Mechanism of autoregulation of GFR

GFR is auto-regulated by *"tubuloglomerular feedback"*

1. Afferent arteriolar vasodilator feedback mechanism

Too little flow of glomerular filtrate into the tubules causes decreased sodium and chloride ion concentration at the macula densa.

The decreased ionic concentration causes afferent arteriolar dilation

This in turn allows increased blood flow into the glomerulus, which increases the glomerular pressure

The increased glomerular pressure as well as the increased glomerular blood flow increases the GFR towards the required level.

REGULATION OF GLOMERULAR FILTRATION

2. Efferent arteriolar vasoconstrictor feedback mechanism:

- A low GFR causes excess reabsorption of sodium and chloride ions in the ascending limb of the loop of Henle, reducing the ionic concentration at the macula densa.
The low concentration of ions causes the juxtaglomerular cells to release renin from their granules.
- The renin causes formation of angiotensin II.
- The angiotensin II constricts the efferent arterioles, which causes the pressure in the glomerulus to rise.
- The increased pressure then causes the glomerular filtration rate to return back towards normal.

REGULATION OF GLOMERULAR FILTRATION [SYMPATHETIC NERVOUS SYSTEM]

Regulation	Major Stimulus	Mechanism	Effect on GFR
Sympathetic Nerves (Autonomic)	**Acute fall in systematic blood pressure. Release of norepinephrine**	**Constriction of afferent arterioles**	**Decrease GFR and filtrate volume to maintain blood volume**

REGULATION OF GLOMERULAR FILTRATION [NEURAL REGILATION]

Regulation	Major Stimulus	Mechanism	Effect on GFR
Tubuloglomerular feedback	Rapid increase in Na+ and Cl- In lumen at the macula densa due to increased BP	Decreased release of Nitric Oxide by JGA causing AA constriction	Decrease GFR and filtrate volume

REGULATION OF GLOMERULAR FILTRATION [HORMONAL]

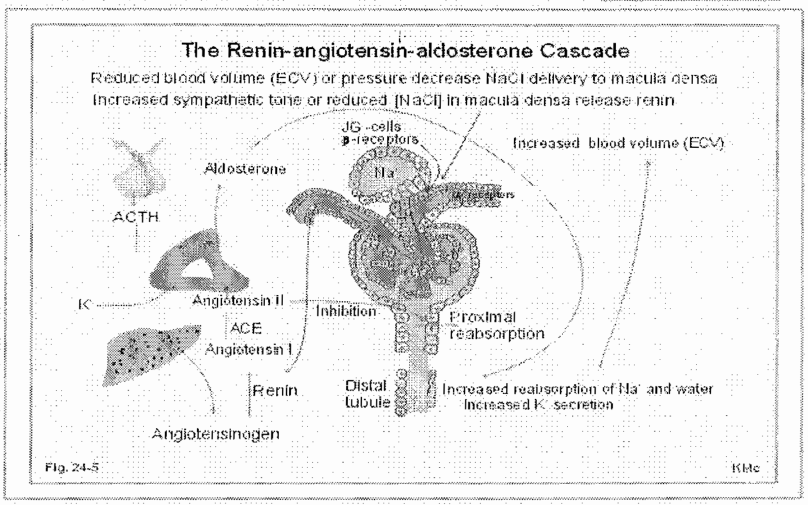
Renin-Angiotensin Mechanism

- Is triggered when the JG cells release renin
- Renin acts on angiotensinogen to release angiotensin I
- Angiotensin I is converted to angiotensin II
- Angiotensin II:
  - Causes mean arterial pressure to rise
  - Stimulates the adrenal cortex to release aldosterone
- As a result, both systemic and glomerular hydrostatic pressure rise

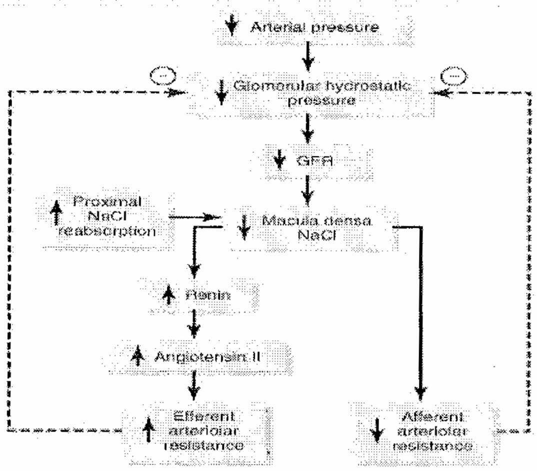
REGULATION OF GLOMERULAR FILTRATION [HORMONAL]

Regulation	Major Stimulus	Mechanism	Effect on GFR
Angiotensin II	**Decreased blood volume or decreased blood pressure**	**Constriction of both afferent and efferent arterioles**	**Decreases GFR**
Atrial natriuretic peptide	**Stretching of the arterial walls due to increased blood volume**	**Relaxation of the mesangial cells increasing filtration surface**	**Increases GFR**

REGULATION OF GLOMERULAR FILTRATION



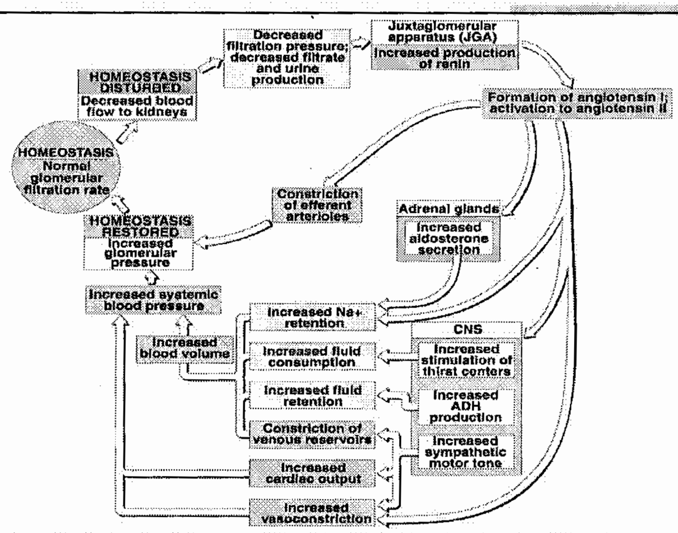
REGULATION OF GLOMERULAR FILTRATION



REGULATION OF GLOMERULAR FILTRATION

- Renin is released to the blood by JGA cells due to decreased renal blood flow or perfusion.
- Renin converts a plasma protein (angiotensinogen) into angiotensin I
- Angiotensin-Converting Enzyme (ACE) in the lungs convertes Angiotensin I into Angiotensin II

REGULATION OF GLOMERULAR FILTRATION RATE



FACTORS AFFECTING GLOMERULAR FILTRATION RATE

Factors affecting filtration rate at the capillary bed:

- Total surface area available for filtration
- Filtration membrane permeability
- Net filtration pressure

- GFR is directly proportional to the NFP
- Changes in GFR normally result from changes in glomerular blood pressure

FACTORS AFFECTING GLOMERULAR FILTRATION RATE

- Changes in renal blood flow
- Changes in glomerular capillary hydrostatic pressure
- Changes in systemic blood pressure
- Afferent or efferent arteriolar constriction
- Changes in hydrostatic pressure in Bowman's capsule
- Ureteral obstruction
- Edema of kidney inside tight renal capsule
- Changes in concentration of plasma proteins: dehydration, hypoproteinemia, etc
- Changes in glomerular capillary permeability , Changes in K_f
- Changes in effective filtration surface area

FACTORS AFFECTING GLOMERULAR FILTRATION RATE

Hormone or Autacoid	Effect on GFR
Norepinephrine	= Decrease GFR
Epinephrine	= Decrease GFR
Endothelin	= Decrease GFR
Angiotensin II	(prevents) Decrease GFR
Endothelial-derived nitric oxide	= Increased GFR
Prostaglandins	= Increased GFR

FACTORS AFFECTING GLOMERULAR FILTRATION RATE

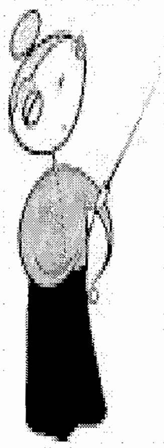
Factors That Can Decrease the Glomerular Filtration Rate

- **Physiological / Patho physiological Causes**
- Renal disease, diabetes mellitus, hypertension
- Urinary tract obstruction (e.g., kidney stones)
- Decreased Renal blood flow, increased plasma proteins
- Deceased arterial pressure (has only small effect due to autoregulation)
- Decreased angiotensin II (drugs that block angiotensin II formation)
- Increased Sympathetic activity, vasoconstrictor hormones (e.g., norepinephrine, endothelin)

FACTORS AFFECTING GLOMERULAR FILTRATION RATE

Increasing Factors	Decreasing Factors
1. Increased renal blood flow	1. Increased plasma colloid osmotic pressure
2. Increased glomerular pressure	2. Increased Bowman's capsule pressure
3. Increased blood pressure	3. Afferent arteriolar constriction
4. Efferent arteriolar constriction	4. Sympathetic stimulation, causing afferent arteriolar constriction.

MEASURING GLOMERULAR FILTATION RATE



MEASURING GLOMERULAR FILTATION RATE GFR

MEASURING GLOMERULAR FILTATION RATE

- The **glomerular filtration rate (GFR)** can be measured in animals and humans by measuring the excretion and plasma level of a substance that is freely filtered through the glomeruli and neither secreted nor reabsorbed by the tubules.
- The amount of such a substance in the urine per unit of time must have been provided by filtering exactly the number of ml of plasma that contained this amount.

SUBSTANCE USED TO MEASURE THE GFR

- Substance must be freely filtered and neither reabsorbed nor secreted in the tubules
- Substance suitable for measuring the GFR should be nontoxic and not metabolized by the body.
- Inulin, a polymer of fructose with a molecular weight of 5200 that meets the criteria in humans and most animals and is extensively used to measure GFR.

MEASURING GLOMERULAR FILTATION RATE

$$U_{IN} = 35 \text{ mg/mL}$$

$$\dot{V} = 0.9 \text{ mL/min}$$

$$P_{IN} = 0.25 \text{ mg/mL}$$

$$C_{IN} = \frac{U_{IN}\dot{V}}{P_{IN}} = \frac{35 \times 0.9}{0.25}$$

$$C_{IN} = 126 \text{ mL/min}$$

THANK YOU